lish peripheral connections, implying a role for NGF and trkA in peripheral axonal targeting (Patel et al., 2000). Clearly, the complete details of axonal targeting of these neurons is likely to involve additional players along with trkA and DRG11. It is nonetheless tempting to speculate that while NGF and TrkA influence peripheral targeting, DRG11 represents the other half of the equation and is specifically required for correct central axonal targeting of nociceptive sensory neurons.

In conclusion, the thorough analysis of *DRG11* knockout mice has shed light on the development of nociceptive neurons, and the complex phenotype of such mice will no doubt prompt many future experiments, including those using conditional gene targeting approaches, aimed at pinpointing the time, place, and mechanism of action of this protein. Placing DRG11 in a molecular pathway will help bridge the gap between development and function in the sensory nervous system. Considering the perinatal lethality of the null genotype on some genetic backgrounds, it is likely that DRG11 plays an interesting role in non-nociceptive cell types as well.

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The Perception of Inferred Action

Our actions, and those of others, are often partly obscured from view. This complicates the sensory inputs that guide motor actions. In this issue of *Neuron*, Umilità and colleagues demonstrate that "mirror neurons" in ventral premotor cortex respond when monkeys observe hidden, but inferred, actions.

In the past decades, neuroscientists have attempted to delineate the functional elements and associated brain regions important for sensory-to-motor integration. Experimental approaches like single cell recordings in monkeys, functional imaging studies in humans, as well as neuropsychological studies on patients have produced a picture of a series of processing steps performed mostly in parietal and frontal cortex. The areas involved appear very similar in humans and monkeys (see, e.g., Bremmer et al., 2001). However, the question of where perception ends and action starts has not been answered yet. Instead, recent experimental evidence argues against a sharp border between the two subsystems. While parietal cortex is considered to be mostly sensory in function (with regard to action preparation), cells whose activity is primarily related to the intention or performance of action have also been described. On the other hand, cells in premotor cortex or the frontal eye fields are not purely related to motor preparation or performance, but can also be driven by pure sensory (visual, tactile, and/or auditory) stimuli. Perhaps, even more intriguingly, cells in a specific part of the macaque sensory-motor system have been described that discharge in relation to action—either performed by the animal itself or being performed by another animal (or the experimenter). These functional properties of the cells have led Rizzolatti, Gallese, and colleagues to coin the term "mirror neurons" (Gallese et al., 1996).

Usually, discharges of these cells, which are located in the ventral portion of the premotor cortex, correlate with the performance or perception of grasping or manipulating an object with either the hand or the mouth. Interestingly, neither visual inspection of the object alone nor imitation of the same action without object is effective in driving the cells. In other words, the discharge of these neurons is strongly related to the "true" performance of action. Functional imaging studies recently demonstrated that a representation of action and/or action perception also exists in humans (Buccino et al., 2001; Iacoboni et al., 1999). Depending on whether perceived actions are object-related or not, parietal and premotor regions (object-related) or only premotor cortex (non-object-related) are activated. Observation of both types of action performed by a mouth, hand, or foot determined a somatotopically organized activation pattern similar to that of the classical motor cortex homunculus. Furthermore, imitation of a previously observed action evoked higher activity levels than performance of the same movement instructed by spatial or symbolic cues. Thus, in humans as in nonhuman primates, it seems that an internal replica of a perceived action is automatically generated, represented as if the subjects were themselves performing that action.

However, our (as well the monkeys') everyday life is full of action that is at least partly occluded from full vision. For example, watching a pickpocket clearly infers the likely outcome of the action. With their latest study, Umiltà et al. (2001 [this issue of *Neuron*]) further our knowledge about "action perception" significantly and provide now strong evidence for the capability of mirror neurons to encode not only fully perceived but even visually inferred action. In their experiments, responses of previously selected mirror neurons were compared in conditions when an experimenter grasped an object fully visible to the monkey ("full vision condition") and when the experimenter performed the very same grasping movement hidden partly behind an opaque occluder, out of the monkey's view ("hidden condition"). About half of the neurons were active in both conditions. Hence, these neurons' activity indicates the perception of *inferred* action. In control experiments, the same neurons were tested when the experimenter grasped (under full or hidden view) a nonexisting target, i.e., an object that previously had been removed and whose removal was visible to the animal. Neurons did not respond under these latter conditions, although the visual information available for the monkey in the two hidden conditions (with and without object) were identical. Simultaneous recordings of the experimenter's hand trajectories as well the monkey's eye movements convincingly showed that these neurons selectively responded to grasping of an object, whether visible or not.

Umiltà, Rizzolatti, and colleagues demonstrate with their study that the encoding of biologically plausible action and/or inferred "events" or "states" is a major capability of primate cortical information processing. Their finding is well in line with previously reported activation patterns in different cortical regions. One such example is the activation of neurons in the anterior portion of the macaque STS during the perception of biological motion. Neurons in this area respond selectively to the view of a walking person (Oram and Perrett, 1996). Concerning hidden action, the disappearance of a walking figure is accompanied by a much stronger activation if this disappearance is biologically plausible rather than caused, e.g., by closing the shutter of the projection system. In humans, recent functional imaging studies revealed the existence of an area dedicated to the encoding of an inferred human walker, i.e., a walking person as observed by Johannson-like point light displays (Grossman et al., 2000). Although this activation was also located in the region of the STS, functional and anatomical equivalence between both territories in humans and monkeys remains to be determined.

Involvement in the perception of inferred action has also been demonstrated for neurons in monkey posterior parietal cortex. Assad and Maunsell (1995) tested the capability of neurons in this part of the monkey brain to infer the motion of visual targets. In blocks of trials, the moving stimulus disappeared from the screen to reappear a couple of hundred milliseconds later either at the same position (as if it had not moved at all) or at a given distance (as if it had passed behind an occluder). A considerable portion of neurons responded only in the latter condition (invisible movement behind an occluder), although the visual stimulus was identical in both conditions. Activity of these neurons was considered to constitute a generalized representation of target motion.

The inference of "still being there" is reflected in a considerable portion of neurons in monkey ventral premotor cortex, as shown by Graziano, Hu, and Gross (Graziano et al., 1997). These authors showed that neurons in PMv discharge in relation to the presence of an object of interest in near extrapersonal space. Neurons continue to fire in darkness, i.e., when the object is no longer visible, if the monkey can presume that the object is still there. Yet, if the object is previously removed and the monkey knows about this removal, these neurons no longer discharge. One may speculate that these neurons described by Graziano et al. could provide the sensory information necessary for the population of neurons described in the present study. Although the crucial part of the action is hidden behind an occluder, animals can infer that objects that were grasped for behind the occluder are still there.

The encoding of the perception of inferred action therefore seems to constitute a basic principle in cortical information processing and sensory-to-motor transformation. Furthermore, it seems to be organized anatomically in a very similar manner in humans and nonhuman primates. Yet, even if one accepted the proposed homology between the delineated part of the macaque ventral premotor cortex and the human Broca region, it would nevertheless remain to be determined whether mirror neurons play an important role in the recognition of phonetic gestures and also language, as suggested recently (Rizzolatti and Arbib, 1998).

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